IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant(s):	Harras, *et al.*	Group Art Unit: 1647
Application No.:	09/703,253	Examiner: R. Landsman
Filed:	10/31/2000	
Title:	Sequences Encoding Human ATP-binding Cassette Transporter Proteins	Atty. Docket No. LEX-0081-USA

APPEAL BRIEF

Mail Stop Appeal Brief
Commissioner for Patents
Alexandria, VA 22313

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APPEAL BRIEF

Sir:

Appellants hereby submit an original and two copies of this Appeal Brief to the Board of Patent Appeals and Interferences ("the Board") in response to the December 18, 2002 (Paper No. 17). The Notice of Appeal was timely submitted on March 13, 2003, and was received in the Patent and Trademark Office ("the Office") on March 18, 2003. This Appeal Brief is timely submitted in light of the concurrently filed Petition for an Extension of Time of four months to and including September 1, 2003 and authorization to deduct the fee as required under 37 C.F.R. § 1.17(a)(4) from Appellants' Representatives' deposit account. The Commissioner is also authorized to charge the fee for filing this Appeal Brief (**$160.00**), as required under 37 C.F.R. § 1.17(c), to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

Appellants believe no fees in addition to the fee for filing the Appeal Brief and the fee for the extension of time are due in connection with this Appeal Brief. However, should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason related to this communication, the Commissioner is authorized to charge any underpayment or credit any overpayment to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

I. REAL PARTY IN INTEREST

The real party in interest is the Assignee, Lexicon Genetics Incorporated, 8800 Technology Forest Place, The Woodlands, Texas, 77381.

II. RELATED APPEALS AND INTERFERENCES

Appellants know of no related appeals or interferences.

III. STATUS OF THE CLAIMS

The present application was filed on October 31, 2000, claiming the benefit of U.S. Provisional

Application Number 60/163,018, which was filed on November 2, 1999, and included original claims 1-4.

The Examiner issued a Restriction and Election Requirement separating the original claims into three separate and distinct inventions, and in a telephone conversation Appellants elected of Group I (claims 1-2), with traverse, for prosecution on the merits.

A First Official Action, was issued on December 19, 2001 ("the First Action" Paper No: 11), Claims 1-2 were rejected under 35 U.S.C. § 101, due to the alleged lack of patentable utility, claims 1-2 were also rejected under 35 U.S.C. § 112, first paragraph, as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, claim 2 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, claim 1 is rejected under 35 U.S.C. § 102(b) as allegedly being anticipated and claims 3-4 were withdrawn from further consideration by examiner as being drawn to a non-elected invention.

In a response to the First Official Action, submitted to the Office on April 19, 2002 ("response to the First Action"), Appellants acknowledged the Restriction and Election Response and amended claim 2 to further improve its clarity.

A Second Official Action, was issued on July 9, 2002 ("the Second Action": Paper No 14), claims 1-2 were maintained under 35 U.S.C. § 101, due to the alleged lack of patentable utility, rejection of claims 1-2 was also maintained under 35 U.S.C. § 112, first paragraph, as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, rejection of claim 2 was maintained under 35 U.S.C. § 112, second paragraph, as allegedly indefinite, the rejection to Claim 1 was withdrawn under 35 U.S.C. § 102(b), but claim 1 was rejected under 35 U.S.C. § 102(a) as allegedly being anticipated.

In a response to the Second Official Action, submitted to the Office on November 11, 2002 ("response to the Second Action"), Appellants amended Claim 1 and new claims 5-7 were added to further improve its clarity and Claim 2 was canceled without prejudice and without disclaimer.

A third and Final Official Action, was issued on December 18, 2002 (the "Final Action" : Paper No. 17), in which rejection of claims 1 and 5-7 was maintained under 35 U.S.C. § 101 and

35 U.S.C. § 112, first paragraph and in view of Appellants amendments to the claim, the rejection of Claim 1 was withdrawn under 35 U.S.C. § 102(a).

In a response to the Final Action, submitted on April 18, 2003 ("response to the Final Action") Appellants again addressed the outstanding rejections of claims 1 and 5-7.

An Advisory Action ("the Advisory Action") was mailed on May 5, 2003, maintaining the rejection of claims 1 and 5-7 were maintained under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph, as one skilled in the art clearly would not know how to use the skilled invention. A copy of the appealed claims is included below in the Appendix (Section IX).

IV. STATUS OF THE AMENDMENTS

For the purposes of Appeal Appellants believe that no outstanding amendments exist.

V. SUMMARY OF THE INVENTION

The present invention relates to Appellants' discovery and identification of novel human sequences that encodes a novel isoform of an ATP-binding cassette transporter protein, a class of proteins that are well known to be involved in mammalian multi-drug resistance(Page 2, lines 7-8). The specification details a number of uses for the presently claimed polynucleotide sequences, including the detection and diagnosis of human disease (page 12) as well as to therapeutically augment the efficacy of chemotherapeutic agents used in the treatment of breast or prostate cancer (page 14, lines 4-6) . The sequences of the present invention are noted to be expressed in prostate (page 3, line 10). Additional uses include assessing temporal and tissue specific gene expression patterns (specification at page 5, line 15-18), particularly using a high throughput "chip" format (specification at page 5, line 19-22), mapping the sequences to a specific region of a human chromosome and identifying protein encoding regions and determining the genomic structure (specification at page 8, lines 11-16). As a still further example of utility is the use of the present sequences in such diagnostic assays (at least at page 14, line 1) as those associated with identification of paternity and forensic analysis, among others. The

sequences of the present invention have particular utility as the application as filed identified several polymorphisms (page 13, lines 16-25).

VI. ISSUES ON APPEAL

1. Do claims 1, and 5-7 lack a patentable utility?
2. Are claims 1 and 5-7 unusable by a skilled artisan due to a lack of patentable utility?

VII. GROUPING OF THE CLAIMS

For the purposes of the outstanding rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, the claims will stand or fall together.

VIII. ARGUMENT

A. Do Claims 1 and 5- 7 Lack a Patentable Utility?

The Final Action first rejects claims 1 and 5 - 7 under 35 U.S.C. § 101, as allegedly lacking a patentable utility due to not being supported by either a specific and substantial utility or a well-established utility, this rejection is maintained in the Advisory Action.

Appellants strongly disagree, as the specification details a number of specific and substantial utilities for the presently claimed polynucleotide sequences which encode a novel isoform of an ATP-binding cassette transporter protein, a class of proteins that are well known to be involved in mammalian multi-drug resistance(Page 2, lines 7-8). The specification details a number of uses for the presently claimed polynucleotide sequences, including the detection and diagnosis of human disease (page 12) as well as to therapeutically augment the efficacy of chemotherapeutic agents used in the treatment of breast or prostate cancer (page 14, lines 4-6) . The sequences of the present invention are noted to be expressed in prostate (page 3, line 10). Additional uses include assessing temporal and tissue specific gene expression patterns (specification at page 5, line 15-18), particularly using a high throughput "chip" format (specification at page 5, line 19-22), mapping the sequences to a specific region of a human chromosome and identifying protein encoding regions and determining the genomic

structure (specification at page 8, lines 11-16). As a still further example of utility is the use of the present sequences in such diagnostic assays (at least at page 14, line 1) as those associated with identification of paternity and forensic analysis, among others. The sequences of the present invention have particular utility as the application as filed identified several polymorphisms (page 13, lines 16-25).

Appellants would like to invite the Board's attention to the fact that a sequence sharing 94% identity at the nucleic acid level with the sequences of the present invention is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Appellants* as ATP-binding cassette, sub-family C, member 11 isoform a; multi-resistance protein 8 (GenBank accession number NP_115972; **abstrac**t, alignment and GenBank report provided in **Exhibit A**) and as ATP-binding cassette, sub-family C, member 11 isoform b; multi-resistance protein 8 (GenBank accession number NP_660187; **abstrac**t, alignment and GenBank report provided in **Exhibit B**) . The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given this GenBank annotation, there can be little question that those skilled in the art would clearly believe that Appellants' sequence is a novel human isoform of the ATP-binding cassette, sub-family C, member 11; multi-resistance protein 8. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Advisory Action (at page 2, lines 6-7), states that "post filing references can only be used to support an asserted utility in the specification. Appellants have only disclosed that in their specification that the protein of the present invention was believed to be an MDR protein." and that Appellants did not know the identity of the protein encoded by the sequences of the of present invention "thereby supporting the Examiner's position that utility was not known at the time of filing." However, Appellants respectfully submit that the issue with regards to 35U.S.C, section 101 is one of utility, not identity or nomenclature and that the legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. The application as filed clearly describes the current invention as a novel human transporter protein (*inter alia,* title, page 1) and the function of transporter proteins as integral

membrane proteins that mediate or facilitate the passage of materials across the lipid bilayer (page 1, lines 26-28) and identifies their role as a mechanism of drug resistance wherein diseased cells using cellular transporter systems to export chemotherapeutic agents from the cell (page 1, line 30-33) and later in the specification asserts a utility in augmenting the efficacy of chemotherapeutic agents used in the treatment of breast or prostate cancer (specification at page 14, lines 8-10).

Appellants have asserted that the present invention is a human transporter protein, and provided evidence that the sequences of the present invention indeed encode a transporter protein, in particular, a variant that encodes and isoform of the ATP-binding cassette, sub-family C, member 11; multi-resistance protein 8. In light of the well-established fact that ATP-binding cassette transporters are known to the art to be frequently associated with multiple drug resistance by cancer cells and that mutations in these genes can cause accelerated removal of chemotherapeutic agents, it is clear the present invention has utility. Appellants have further asserted that similar MDR encoding sequences, uses, and applications that are germane to the proteins encoded by the sequences of the present invention, were described in issued U.S. Patents Nos. 5,198,344 and 5,866,699 which were incorporated by reference in their entirety into the present application.

The well-established utility of the class of transporter proteins encoded by the sequences of the present invention is further evidenced by the NCBI LocusLink summary for ABCC11 genetic locus.

> "The protein encoded by this gene is a member of the superfamily of ATP-binding cassette (ABC) transporters. ABC proteins transport various molecules across extra- and intra-cellular membranes."

> "This ABC full transporter is a member of the **MRP subfamily which is involved in multi-drug resistance. It is expressed at low levels** in all tissues, except kidney, spleen, and colon. This gene and family member ABCC12 are determined to be derived by duplication and are both localized to chromosome 16q12.1. Their chromosomal localization, potential function, and expression patterns identify them as candidates for paroxysmal kinesigenic choreoathetosis, a disorder characterized by attacks of involuntary movements and postures,

chorea, and dystonia. Multiple alternatively spliced transcript variants have been described for this gene."

(http://www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=85320)

Clearly the utility of ABCC 11 transporter proteins, and thus logically the sequences of the present invention which encode an ABCC11 transporter protein isoform, have a very well established utility that is readily recognized by those of skill in the art.

In the Second Official Action (Paper No.14) references, Tammur *et al.* **(Exhibit C)** and Yabuuchi *et al.* **(Exhibit D)** are used to attempt to discredit Appellants' assertion of utility. However these publications support rather than dispute Appellants assertion that the present invention has utility and is a splice variant of ABCC11. For example, Tammur *et al*, in the final paragraph of the introduction (page 90, 4th paragraph), state that they had undertaken a long-term project of cloning new human ABC transporters and linking them to various disease phenotypes and have identified ABCC11 and ABCC12 as two such members. Thus, clearly, Tammur et al., recognize the value and utility of ABCC11 and ABCC12 and their association with human diseases. In addition, with regard to function, Tammur *et al.*, state on page 93, lines 8-10 that "it would be reasonable to suggest that ABC11 and ABCC12 could share functional similarities with ABCC4 and ABCC5." Said function being recognized by the art as the transport of organic anions, nucleotide analogs and cyclic nucleotides. Thus rather than contradicting the utility of the present invention the conclusions of Tammur *et al.* support the position that those of skill in the art would recognize Appellants' asserted utility of the present invention as credible.

Yabuuchi *et al.* clearly supports Appellants' assertion that the present invention is a splice variant of ABCC11, for there appear to be many such variants. And although these authors speculate that "splice variants may represent diverse biological functions" (emphasis added), this speculation is not supported by any data or based on any fact or reference and thus appears to be pure speculation , "Therefore, it is of interest to know whether some of these splice variants...represent biological

functions" (pg 937, lines 17-19). However, Yabuuchi *et al.* also recognize in their concluding remarks the utility of ABCC11 with regard to human disease and therefore also indicate that Appellants' utility assertions as credible. Further recognition of the utility of ABCC11 sequences is provided by other scientific publications, such as that of Turriziani, *et al.*, (Impaired 2',3'-dideoxy-3'-thiacytidine accumulation in T-lymphoblastoid cells as a mechanism of acquired resistance independent of multidrug resistant protein 4 with a possible role for ATP-binding cassette C11, Biochem. J. 368, 325-332 ,2002: **Exhibit E**). Turriziani, *et al.*, describe the finding that increased expression of ATP-binding cassette C11 (ABCC11) was observed in the CEM 3TC cells and that the decreased 3TC accumulation in the CEM 3TC might be due to the upregulation of ABCC11.

Clearly evidence supports Appellants' assertions that the sequences of the present invention which encode a novel human transporter protein,(an isoform of the ATP-binding cassette, sub-family C, member 11; multi-resistance protein 8) have well established utility that is recognized by those of skill in the art.

Furthermore, this situation parallels Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when there is no reason to doubt the asserted utility of a full length sequence (such as the presently claimed sequence) that has a similarity to a protein having a known function. In the Analysis portion of Example 10 it states that "Based on applicant's disclosure and the results of the PTO search, there is no reason to doubt the assertion that SEQ ID NO:2 encodes a DNA ligase . Further DNA ligases have a well-established use in the molecular biology art based on this class of proteins ability to ligate DNA. .....Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed..... Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made."

The present case is similar to that presented in Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55). In the present case it is clear that the sequences of the present invention encode an ATP-binding cassette (ABC) transporter. ATP-binding cassette (ABC) transporters have a well-established utility. "Note that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed...Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made." Thus the rejection of the presently claimed invention under a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph utility rejection should be overruled.

The Advisory action also discounts Appellants' assertion regarding the use of the presently claimed polynucleotides on DNA gene chips, based on the position that such a use would allegedly be generic. Further, these Actions seem to be requiring Appellants to identify the biological role of the nucleic acid or function of the protein encoded by the presently claimed polynucleotides before the present sequences can be used in gene chip applications that meet the requirements of § 101. Appellants respectfully point out that knowledge of the exact function or role of the presently claimed sequence is not required to track expression patterns using a DNA chip. As set forth in at least Appellants Response to Final, given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications.

Clearly, the claimed sequences provide a specific marker of the gene encoding an ABC transporter protein and provide a unique identifier of the corresponding gene in the human genome. Such specific markers are targets for discovering drugs that are associated with human kidney disease, such as congenital nephrotic syndrome. Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as the specification details at least on page 5, line 19-22. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, exemplified by U.S. Patent Nos. 5,445,934 (**Exhibit F**), 5,556,752 (**Exhibit G**), 5,744,305 (**Exhibit H**), as well as more recently issued U.S. Patent Nos. 5,837,832 (**Exhibit I**), 6,156,501 (**Exhibit J**) and 6,261,776 (**Exhibit K**).

The Board is further requested to consider that, given the huge expense of the drug discovery process, even negative information has great "real world" practical utility. Knowing that a given gene is not expressed in medically relevant tissue provides an informative finding of great value to industry by allowing for the more efficient deployment of expensive drug discovery resources. Such practical considerations are equally applicable to the scientific community in general, in that time and resources are not wasted chasing what are essentially scientific dead-ends (from the perspective of medical relevance). Clearly, compositions that enhance the utility of such DNA gene chips, such as the presently claimed sequences encoding ATP-binding cassette (ABC) transporters, must in themselves be useful. Moreover, the presently described ABC transporter provides uniquely specific sequence resources for identifying and quantifying full length transcripts that were encoded by the corresponding human genomic locus. Accordingly, there can be no question that the described sequences provide an exquisitely specific utility for analyzing gene expression.

Additionally, only a small percentage of the genome (2-4%) actually encodes exons, which in turn encode amino acid sequences. Thus, not all human genomic DNA sequences are useful in such gene chip applications. This further discounts the Examiner's position that such uses are "generic". The present claims clearly meet the requirements of 35 U.S.C. § 101. It has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971).

Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company, Rosetta Inpharmatics, was viewed to have such "real world" value that it was acquired by large pharmaceutical company, Merck & Co., for substantial

sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304; **Exhibit L**). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153; **Exhibit M**). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

As a still further example of utility is the use of the present sequences in such diagnostic assays (at least at page 14, line 1) as those associated with identification of paternity and forensic analysis, among others. The sequences of the present invention have particular utility as the application as filed identified several polymorphisms (page 13, lines16-25). This is also not a case of a potential utility. Appellants respectfully submit that even in the worst case scenario, the described polymorphisms are each useful to distinguish 50% of the population (in other words, the marker being present in half of the population) and that the ability of a polymorphic marker to distinguish at least 50% of the population is an inherent feature of any polymorphic marker, and this feature is well understood by those of skill in the art. Appellants note that as a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988). Appellants support for Appellants' assertion of utility is provided by the fact that the skilled artisan would readily recognize and easily believe that the presently described polymorphic markers could be useful in forensic analysis. The fact that forensic biologists use polymorphic markers such as those described by Appellants every day provides more that ample support for the assertion that forensic biologists would also be able to use the specific polymorphic markers described by Appellants in the same fashion. Therefore, again it is clear that the sequences of the present invention have utility.

Given the physiologic activity and importance of ABC transporters known to those of skill in the art, those of skill in the art would readily appreciate the importance of tracking the expression of the genes encoding the described proteins, particularly due to well established role of ABC transporters in drug resistance in cancer cells. In the present case this apparent utility is further bolstered by the expression of the sequences of the present invention in the prostate, a tissue which when involved in cancer often under goes multiple drug resistance. The use of the claimed polypeptide in an array for screening purposes Appellants respectfully point out that nucleic acid sequences have the greatest specific utility in gene chip applications once the role of the sequence has been identified, as have tissues of interest, as in the present case. Once the role of the particular nucleic acid is known, the level of gene expression has and even greater significance. By identifying the physiological activity role of the claimed sequence, the claimed sequence has a far greater utility in gene chip applications that just any random piece of DNA. Appellants respectfully submit that **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, is distinct from the requirement for a **unique** utility, which is clearly an improper standard. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991; "*Carl Zeiss*"):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Therefore, just because other nucleic acid sequences find utility in gene chip applications does not mean that the use of Appellants' sequence in gene chip applications is not a specific utility. Furthermore, the requirement for a unique utility is clearly not the standard adopted by the Patent and Trademark Office. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, such as cancer and bacterial or viral infections, just to name a few particular examples, because examples of each of these have already been described and patented. All batteries have the exact same utility - specifically, to provide power. All automobile tires have the exact same

utility - specifically, for use on automobiles. All golf balls and golf clubs have the exact same utility - specifically, use in the game of golf. All cancer treatments have the exact same utility - specifically, to treat cancer. All anti-infectious agents have the exact same broader utility - specifically, to treat infections. However, only the briefest perusal of virtually any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

Further evidence of utility of the presently claimed polynucleotide, although only one is needed to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), is the specific utility the present nucleotide sequence has in determining the genomic structure of the corresponding human chromosome (specification at page 14, lines 9-10), for example mapping the protein encoding regions as described in the specification (page 3, line 26-29) and evidenced below. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequence. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Only a minor percentage of the genome actually encodes exons, which in turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that

specifically defines that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Appellants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence supporting the Appellants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra at* pp. 1317-1321, including Fig. 11 at pp.1324-1325), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article.

As still further evidence supporting Appellants' assertions of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome and identification of functionally active intron/exon splice junctions is the information provided in **Exhibit N**. This is the result of a blast analysis using SEQ ID NO:23 of the present invention when compared to the identified human genomic sequence. This result indicates that the sequence of the present invention is encoded by 25 exons spread non-contiguously along a region of human chromosome 16, which is contained within represented by clone, AC0076005. Thus clearly one would not simply be able to identify the 25 protein encoding exons that make up the sequence of the present intention from within the large genomic sequence. Nor, would one be able to map the protein encoding regions identified specifically by the sequences of the present invention without knowing exactly what those <u>specific</u> sequences were.

Rather, the question of utility is a straightforward one. As set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be <u>totally incapable</u> of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992),

emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

In *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of

> pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted. In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (C.C.P.A. 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Finally, with regards to the issue of due process, while Appellants are well aware of the new Utility Guidelines set forth by the USPTO, Appellants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Appellants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Board is invited to review U.S. Patent Nos. 5,817,479 (**Exhibit O**), 5,654,173 (**Exhibit P**), and 5,552,281 (**Exhibit Q**; each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (**Exhibit R**; which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner

seems to be requiring. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section VIII(B), below), Appellants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Appellants agree that each application is examined on its own merits, Appellants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Given the rapid pace of development in the biotechnology arts, it is difficult for the Appellants to understand how an invention fully disclosed and free of prior art at the time the present application was filed, could somehow retain *less* utility and be *less* enabled than inventions in the cited issued U.S. patents (which were filed during a time when the level of skill in the art was clearly lower). Simply put, Appellants invention is *more* enabled and retains *at least as much* utility as the inventions described in the claims of the U.S. patents of record. Thus, holding Appellants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, Appellants submit that the rejection of claims 1 and 5-7 under 35 U.S.C. § 101 must be overruled.

B. Are Claims 1 and 5-7 Unusable Due to a Lack of Patentable Utility?

The Final Action and Advisory Action maintain the rejection of claims 1 and 5-7 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by either a clear asserted utility or a well-established utility.

The arguments detailed above in **Section VIII(A)** concerning the utility of the presently claimed sequences are incorporated herein by reference. As the Federal Circuit and its predecessor have determined that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph, have the same basis, specifically the disclosure of a credible utility (*In re Brana, supra*;

In re Jolles, 628 F.2d 1322, 1326 n.11, 206 USPQ 885, 889 n.11 (CCPA 1980); *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971)), Appellants submit that as claims 1 and 5-7 have been shown to have "a specific, substantial, and credible utility", as detailed in **Section VIII(A)** above, the present rejection of claims 1 and 5-7 under 35 U.S.C. § 112, first paragraph, cannot stand.

Appellants therefore submit that the rejection of claims 1 and 5-7 under 35 U.S.C. § 112, first paragraph, must be overruled.

IX. APPENDIX

The claims involved in this appeal are as follows:

1. An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:23.

5. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence of SEQ ID NO:24.

6. An expression vector comprising a nucleic acid sequence encoding the amino acid sequence of SEQ ID NO: 24.

7. A cell comprising the expression vector of Claim 6.

X. CONCLUSION

Appellants respectfully submit that, in light of the foregoing arguments, the Final Action's conclusion that claims 1 and 5-7 lack a patentable utility and are unusable by the skilled artisan due to a lack of patentable utility is unwarranted. It is therefore requested that the Board overturn the Final Action's rejections.

Respectfully submitted,

September 18, 2003
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